UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,341	03/22/2001	Nancy J. Bump	BBC-069	4413

7590 07/26/2004

Gayle B. O'Brien
Abbott Bioresearch Center
100 Research Drive
Worcester, MA 01605-4314

EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/815,341	BUMP ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 July 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *08 July 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *21-27,32 and 33*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): The claim objection of claim 32 has been overcome. The 35 USC 112, second paragraph rejection has been overcome.

Continuation of 5. does NOT place the application in condition for allowance because: the 35 U.S.C. 112, first paragraph, lack of scope of enablement and lack of written description rejections, and the 35 USC 103 rejections are maintained.

Lack of scope of enablement, 35 USC 112, 1st paragraph
Applicants state they have exemplified all steps in instant claim 21. This is acknowledged for using the atomic coordinates for residues 802-1124 of Tie-2 and Inhibitor complex. However, this exemplification does not satisfy enablement issues of obtaining atomic coordinates of an unbound version of a Tie-2 polypeptide or atomic coordinates of the complete polypeptide of Tie-2 and Inhibitor III complex. Due to the unpredictability of the science of protein crystallization, Applicants are only enabled for the specific atomic coordinates addressed in the specification, claims, and drawings, as originally filed. Applicants state the method of instant claim 21 is directed to a first step of obtaining the atomic coordinates of a crystal of a polypeptide comprising the catalytic domain of a Tie-2 protein and have listed the approximate residues involved in the catalytic domain. It is noted that the way instant claim 21 is worded, step (a) broadly encompasses atomic coordinates of any crystal of a polypeptide comprising such a domain which includes more types of atomic coordinates sets of crystallized polypeptides than listed in the instant application. Applicants only provide enablement for the atomic coordinates referred to in the instant application. Applicants state the Examiner must show specific reasons why other embodiments within the full scope of claim 21 would not work, rather than merely alleging the unpredictability of the art. The Drenth reference provides proper documentation to illustrate the unpredictability in this art and MPEP section 2164.03 addresses how such unpredictability should be handled in the examination of an application directed to an unpredictable art. Applicants state the crystallization of proteins is not unpredictable. This statement is found unpersuasive when viewed in context of the Drenth reference. Applicants state the crystallization of proteins does not entail undue experimentation. This statement is found unpersuasive as unpredictability is one of the factors to determine such undue experimenation. Applicants state the amount of experimentation required for the instant invention is routine. This statement is found unpersuasive due to the unpredictability involved in the art of protein crystallization such that one of skill in the art could not reasonably expect to obtain the other coordinates encompassed in the instant claims except for the ones listed in the specification that are known to already be obtainable. Applicants cite the Crystallization of Membrane Proteins reference to show examples of how one crystallizes a protein and the possible need to adjust variable parameters to obtain a crystal. This variability and fine tuning demonstrate that the protein crystallization art has many variables to address. The Drenth reference states that such a trial and error procedure has unpredictable results. Due to the unpredictability of protein crystallization, this rejection is maintained.

Lack of written description, 35 USC 112, 1st paragraph
Applicants state they have crystallized approximately 95% of the cytoplasmic domain of Tie-2 with only 30 amino acids missing from the N-terminus of Applicants' crystal. The atomic coordinates of this crystal have adequate written description. Applicants have not provided atomic coordinates for the unbound Tie-2 polypeptide or for the entire Tie-2 polypeptide and Inhibitor III complex which are encompassed in the "comprising" language used on line 3 of claim 21. Therefore, Applicants do not seem to have possession of these additional atomic coordinates. Applicants state they have reduced the instant invention to practice. They have support for reducing the invention to practice only regarding the atomic coordinates listed in the specification. Applicants state examples representative of a genus are sufficient for a claim directed to a chemical genus. According to MPEP section 2164.03, this does not apply when results are unpredictable. Applicants state their invention is directed to a method. This is acknowledged. However, the method includes a step of obtaining atomic coordinates from a crystal which is where the unpredictability of the the invention exists. With such unpredictability, only the specific examples provided in the specification have adequate written support

35 USC 103 rejections

Regarding the rejection of claims 21, 22, and 26 under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (P/N 6,160,092), in view of In re Gulack (703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983)), Applicants state Chen et al. describe a method of identifying a drug that affects the ability of STAT to induce expression of a gene whereas the instant invention is directed to a method of identifying a compound which is the inhibitor of a Tie-2 protein. Chen et al. describe on column 4, lines 56-60, that diminishes (antagonist) the actions of STAT which represents an inhibitor. Applicants state Chen et al do not teach or suggest the step of obtaining the atomic coordinates of a Tie-2 protein. This statement is found unpersuasive as the atomic coordinates are considered nonfunctional descriptive material, such that Chen et al. in view of In re Gulack suggests this step. Applicants state that claim 21 is directed to a method. This is acknowledged. It is the fact that this method contains nonfunctional descriptive material that an In re Gulack rejection has been set forth. Applicants state the atomic coordinates are functionally related to both the crystal polypeptide, from which they are obtained, and the compound which is identified based on the atomic coordinates. This statement is found unpersuasive as the functional interrelationship with the way in which computer processes are performed does not exist with the descriptive material in the instant application.

Regarding the rejection of claims 21-27 under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (P/N 6,160,092), in view of In re Gulack (703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983)), In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594), and Ziegler (P/N 5,447,860), Applicants reiterate the arguments described in the paragraph above which were found unpersuasive and addressed above. Applicants continue by stating the Ziegler patent refers to the biological ligand of Tie that binds to the extracellular domain, and not the small molecular ligands that bind to the catalytic domain of Tie-2. This statement is found unpersuasive as the instant claims, such as instant claim 21, do not state that the compound must bind to the catalytic domain of Tie-2. Instead the compound must simply bind to one or more active subsites (note the first line of step (c) in instant claim 21 does not mention to what these subsites belong). Applicants state Ziegler does not teach or suggest identifying compounds to inhibit a Tie-2 protein. Every reference in a 35 USC 103 rejection need not recite every limitation which is why the references are combined with other references if there is proper motivation to do so. Applicants fail to offer support as to why the motivation in this rejection would be considered improper; therefore, the rejection with its motivation to combine references is maintained.

Regarding the rejection of claims 21-27 under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (P/N 6,160,092), in view of Vikkula et al. (Cell, 1996, Volume 87, pages 1181-1190) and In re Best (195 2USPQ 430) and In re Fitzgerald (205 USPQ 594), Applicants state

the Examiner has not presented a prima facie case of obviousness. This is found unpersuasive as the limitations in the instant claims were adequately addressed with motivation to combine references. Applicants state Vikkula et al. would not be looked at for guidance on a method to identify compounds that inhibit Tie-2 proteins. This is found unpersuasive as motivation to combine references is provided by the Chen et al. reference. Chen et al. suggest finding inhibitors (see antagonist discussion described two paragraphs, supra), identifying agents that interact with a protein and various modifications of their invention (col. 38, lines 2-5) to search for new modulators and possible drug candidates (col. 3, lines 5-9 and col. 4, lines 32-38). Applicants state the Examiner has not provided any motivation to modify Vikkula et al. and that Vikkula et al. does not teach all of the limiations of the Applicants' claims. This is found unpersuasive as Chen et al. provide motivation and Applicants have not provided any sound reasoning as to why the Chen et al. motivation would be considered improper. Furthermore, Vikkula et al. does not need to teach all of the limitations of the instant invention which is why it is in a 35 USC 103 rejection and not a 35 USC 102 rejection. All of the limitations of the instant invention are addressed with the references and case law provided in the rejection. Applicants state the same arguments presented in the first two 35 USC 103 rejections apply to this 35 USC 103 rejection. Those arguments are also found unpersuasive for the reasons given in the two paragraphs directly above this one. Therefore, this rejection is maintained.

Ardin H. Marschel 7/22/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER